Patent Application 0 260 148 (hereinafter "Gorman"). Claims 18, 19 and 25 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Jiang, et al. (1997) Gene, 185: 285-290 (hereinafter "Jiang, et al."). Claims 18, 19 and 25 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Blanchard, et al. (1997) Biology of Reproduction, 56: 495-500 (hereinafter "Blanchard, et al."). Claims 18-20, 25 and 26 have been rejected under 35 U.S.C. §102(a) as allegedly anticipated by Eskola, et al. (1998) Molecular and Cellular Endocrinology 139: 143-152 (hereinafter "Eskola, et al."). Claims 18-20, 25 and 26 have been rejected under 35 U.S.C. §102(a) as allegedly anticipated by Ducray, et al. (1998) Steroids 63: 285-287 (hereinafter "Ducray, et al."). Claims 18-26 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman as applied to 18-20, 25 and 26 and further in view of Builder, et al. U.S. Patent No. 5,663,304 (hereinafter "Builder, et al."); Muelin U.S. Patent No. 5,521,070 (hereinafter "Muelin"); Ritter, et al. (1991) J. Biol. Chemistry 266: 1043-1047 (hereinafter "Ritter, et al."); and Ciotti, et al. (1996) Biochemistry 35: 10119-10124 (hereinafter "Ciotti, et al.).

In response to the above rejections, applicant has amended the claims which, when considered with the accompanied comments, is deemed to place the present application in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

Claims 18-26 have been rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite. The Examiner specifically alleges that Claims 18 and 20 recite a coding sequence for a biological factor or intermediate or wherein by the term 'intermediate" is not

defined. In response, and in an effort to expedite favorable prosecution, applicant has deleted the recitation "intermediate" from Claims 18 and 20.

The Examiner has rejected Claim 19 based on the recitation " the vector of Claim 8". Applicant has amended Claim 19 to correct an inadvertent typographical error. Claim 19 now properly depends from Claim 18.

The Examiner has rejected Claim 20 because according to the Examiner, the recitation "signal sequence upstream" could allegedly be interpreted as meaning that there could be two signal sequences, with the second signal sequence being upstream of the native signal sequence of the biological factor. The Examiner further alleges that such recitation is redundant.

In response, and in an effect to expedite favorable prosecution, applicant has amended Claim 20 in accordance with the Examiner's recommendation to delete the recitation "upstream to said coding sequence for a biological factor or intermediate". New Claims 27-31 have been added to further define the subject matter to which applicant is entitled. Support for Claims 27-28 is found throughout the specification and particularly at original Claim 21 and 23, respectively. Support for Claims 29-31 is found throughout the specification and particularly at page 24, lines 15-18, at page 25, lines 17-23 and at page 6, lines 19-23, for example. No new matter has been added.

Accordingly, the rejection of Claims 18-26 under 35 U.S.C. §112, second paragraph is overcome and withdrawal thereof is respectfully requested.

Claims 18-20, 25 and 26 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Gorman. Gorman allegedly teaches vectors and Sertoli cells

comprising the vectors. The Examiner further alleges that the vectors comprise a promoter which is operatively linked to a coding sequence for a biological factor ("factor VIII").

Claims 18, 19 and 25 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Jiang, et al. The Examiner alleges that Jiang, et al. teach a vector comprising a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor (luciferase); and Sertoli cells comprising the vector.

Claims 18, 19 and 25 have been rejected under 35 U.S.C. §102(b) as allegedly anticipated by Blanchard, et al. The Examiner alleges that Blanchard, et al. teach a vector comprising a promoter operatively linked to a coding sequence for a biological factor (lacZ); and Sertoli cells comprising the vector.

Claims 18-20, 25 and 26 have been rejected under 35 U.S.C. §102(a) as allegedly anticipated by Eskola, et al. The Examiner alleges that Eskola, et al. teach a vector comprising a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor (follicle-stimulating hormone receptor, or FSHR); and Sertoli cells comprising the vector.

Claims 18-20, 25 and 26 have also been rejected under 35 U.S.C. §102(a) as allegedly anticipated by Ducray, et al. The Examiner alleges that Ducray, et al. teach a vector comprising a coding sequence for a biological factor (ABP); and Sertoli cells comprising the vector.

Applicant submits that a rejection of a claims under U.S.C. §102(a) or (b) requires that the prior art reference disclose every element of the claim. It is axiomatic that there must be no differences between the subject matter of the claim and the disclosure of the

prior art. The absence from the reference of any claimed element, negates anticipation. Kloster Speedsteel AB v. Crucibile Inc., 793 F2d 1565, 1571, 230 U.S.P.Q. 81, 84 (Fed. Cir. 1986).

Applicant submits that none of the cited references teach or disclose a vector comprising a coding sequence for a biological factor wherein said sequence codes for human factor IX, bilirubin UDP-glucuronosyltransferase, insulin, IL-2, dopamine, GM-CSF, M-CSF or TNF, as presently claimed. Moreover, none of the cited references teach a Sertoli cell comprising the vector which functions in a Sertoli cell operatively linked to a coding sequence for a biological factor wherein the Sertoli cell creates an immunologically privileged site *in vivo*. Therefore, the cited references do not disclose every element of the pending claims. Accordingly, applicant submits that the rejection of Claims 18-20, 25 and 26 under 35 U.S.C. §102(a) and (b) is overcome and withdrawal thereof is respectfully requested.

Claims 18-26 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Gorman and further in view of Builder, et al., Meulien, Ritter, et al. and Ciotti, et al.

The Examiner alleges that Builder et al. teach expression of DNA encoding a desired polypeptide and a suitable host cell appropriate for the expression of the DNA encoding the desired polypeptide. The Examiner also alleges that useful mammalian host cells such as mouse Sertoli cells are contemplated by Builder, et al.

The Examiner further alleges that expression of desired polypeptides include Factor VIIIC and Factor IX. The Examiner concedes that Builder, et al. do not provide

working examples of Sertoli cells comprising vectors encoding factor VIII or factor IX and that Builder, et al. do not specifically mention bilirubin UDP-glucuronosyltransferase.

The Examiner alleges that Muelien, et al. teach that in the sequence coding for Factor IX there is a signal sequence encoded in the cDNA. The Examiner admits that Muelien, et al. do not teach Sertoli cells. Similarly, although Ritter, et al. are alleged to teach the cloning of cDNAs for two bilirubin UDP-glucuronosyltransferases, Ritter, et al. do not teach Sertoli cells. Finally, the Examiner alleges that Ciotti, et al. teach vectors comprising bilirubin UDP-glucuronosyltransferase, but like Muelien, et al., and Ritter, et al., Ciotti, et al. do not teach Sertoli cells. Nevertheless, the Examiner alleges that at the time of the invention, the skilled artisan would have been motivated to express in cells "any biological factor (polypeptide) of interest, especially polypeptides of importance to human biology, such as factor VIII, factor IX or bilirubin UDP-glucuronosyltransferase... so that the polypeptide could be produced and either used for therapeutic purposes or studied in vitro...".

Applicant respectfully submits that the prior art does not provide any suggestion or motivation to make the claimed invention. There is no motivation, teaching or suggestion in the cited references to combine the separate features of Gorman, Builder, et al., Muelein, Ritter, et al. and Ciotti, et al. Such combination does not arrive at the presently claimed invention in any event.

The Examiner alleges that the skilled artisan would have been aware of "teachings of expression of polypeptides in different types of cells, as such references would all be analogous art and different cells that were shown to be successful for expression of biological factors would be art-recognized equivalents of one another". Moreover, the

Examiner alleges that one would have been motivated to use a promoter that functioned in the cells so that the desired polypeptides would be expressed.

Builder, et al. teach expression of DNA encoding a desired polypeptide. Builder, et al. provide no suggestion, motivation or teaching no less any recognition of a Sertoli cell which creates an immunologically privileged site for the biological factor expressed thereby. The secondary references, Muelein, et al., Ritter, et al., and Ciotti, et al., do not even teach Sertoli cells. Applicant submits that the Examiner has taken bits and pieces of Builder, et al., Muelein, et al., Ritter, et al., Ciotti, et al. and Gorman and interpreted such disclosures in a way that was not intended and is not correct. Moreover, the secondary references fail to ameliorate the deficiencies of Builder, et al. and Gorman. Applicant therefore submits that the interpretation urged by the Examiner is too broad given the clear teaching of the references, the Examiner's own admissions and the amendments to the claims.

The rejection of claimed subject matter as obvious under 35 U.S.C. §103(a) in view of the combination of prior art references requires that the suggestion to carry out the claimed invention must be found in the prior art, not in applicants' disclosure. In re Vaeck, 947 F2d 488, 493, 20 U.S.P.Q. 2d 1438, 1442 (Fed. Cir. 1991). In In re Vaeck, the applicant claimed a Bacillus gene in a host cyanobacteria that produced an insecticidal protein. The prior art taught both the gene and the bacterium, but did not teach the combination as described by applicants. The court held the claimed invention was not obvious stating:

> The prior art in this case offers no suggestion, explicit or implicit, of the substitution that is the difference between the claimed invention and the prior art. In re Veack, 947, F2d 495, 20 USPQ 2nd at 1444.

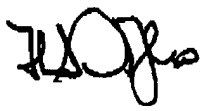
In the present case the Examiner has not met the burden of demonstrating either an explicit or implicit suggestion in the prior art to combine the separate features of Builder, et al., Gorman, Muelein, Ritter, et al. and Ciotti, et al. in order to achieve the claimed invention. There must be an indication in the prior art as a whole to suggest the desirability, and thus the obviousness of making the combination. In re Newell, 891 F2d 899, 901, 13 USPQ 2d 1248, 1250 (Fed. Cir. 1989). There is no such suggestion identified on this record.

Accordingly, the rejection of Claims 18-26 under 35 U.S.C §103(a) is overcome and withdrawal thereof is respectfully requested.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Thus, in view of the foregoing amendments and remarks, it is certainly believed that the subject application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Please cancel Claims 21, 22, 23 and 24 without prejudice.

Claims 18-20 and 25-26 have been amended as follows:

18. (Amended) A vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor [or intermediate] wherein said coding sequence is the coding sequence for human factor IX.

19. (Amended) The vector of Claim [8] 18 further comprising a 3' termination sequence which functions in Sertoli cells.

20. (Amended) The vector of Claim 18 or 19 further comprising a signal sequence coding for a signal peptide, said signal sequence located downstream from said promoter [and upstream to said coding sequence for a biological factor or intermediate].

25. (Amended) A Sertoli cell comprising [the vector of Claim 18 or 19] a vector comprising, in the 5' to 3' direction, a promoter which functions in Sertoli cells, operatively linked to a coding sequence for a biological factor wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

26. (Amended) A Sertoli cell comprising [the vector of Claim 20] a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor and a signal sequence coding for a signal

peptide, said signal sequence located downstream from said promoter, wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

Claims 27-31 have been added as follows:

27. (New) A vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for bilirubin UDP-glucuronosyltransferase (B-UGT).

28. (New) A vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for a biological factor selected from the group consisting of insulin, IL-2, dopamine, GM-CSF, M-CSF or TNF.

29. (New) A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for factor VIII and wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

30. (New) A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for factor IX and wherein said Sertoli cell creates an immunologically privileged site *in vivo*.

31. (New) A Sertoli cell comprising a vector comprising in the 5' to 3' direction a promoter which functions in Sertoli cells operatively linked to a coding sequence for a biological factor wherein said coding sequence is the coding sequence for bilirubin UDP-

glucuronosyltransferase (B-UGT) and wherein said Sertoli cell creates immunologically privileged site *in vivo*.